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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,951	08/20/2001	Nobuhiro Sato	213126US0X	4655

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EXAMINER

FORD, VANESSA L

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 04/26/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/931,951	SATO ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 1-13 and 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-15 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's response to the Restriction requirement filed in Paper No. filed on February 2, 2002 is acknowledged. Applicant's election of Group V with traverse, claim 14, is acknowledged. Claims 1-13 and 15 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The traversal is on the grounds that Groups I-VI are not independent and distinct, therefore the examination of the entire application does not constitute a serious burden. These arguments have been fully considered but are not found to be persuasive for the reasons below:

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each (see MPEP 802.01). In the instant situation, the inventions of Groups I-V are drawn to distinct inventions which are separate products and methods capable of separate manufacture, use or sale as described in the previous Office Action.

Classification of the subject matter is merely one indication of the burdensome nature of the search. The literature search, particularly relevant in this art, is not co-extensive, because for example, Groups I, IV and VI are drawn to different products. Groups II, III and V are drawn to different methods which require different method steps, parameters and endpoints. Clearly different searches and issues are involved in the examination of each Group.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification Objections

2. The specification is objected to because of the following informalities: What appear to be typographical errors. For example, "colomic" which should be changed to "colonic"(page 4, line 10) and "ELIZA" which should be changed to "ELISA" (page 9, line 13). The specification is also objected to because the genus and species of microorganisms are not italicized or underlined, for example *Fusobacterium varium* should be changed to "*Fusobacterium varium*" or "Fusobacterium varium". Applicant is asked to review the specification for the above informalities and correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 14 is drawn to a method of diagnosis of ulcerative colitis.

The specification is only enabled for a method of detecting *Fusobacterium varium* antibodies and not a method of diagnosis of ulcerative colitis.

There are several factors that contribute to the diagnosis of a disease or disorder that are well known in the art. These factors include: 1) the known etiologic agent that causes the disease, 2) the cross reactivity of multiple microorganisms involved in the disease and 3) the immunopathogenesis associated with the disease. The etiologic agent associated with ulcerative colitis is unknown. This is evidenced by Sartor (*Gasroenterology Clinic of North America (UNITED STATES)*, September 1995, 24, p. 475-507). Sartor teaches that ulcerative colitis and Crohn's disease collectively are referred to as inflammatory bowel disease (IBD), are chronic, spontaneously relapsing disorders of unknown cause (see the Abstract). Braegger (*Acta Paediatr Suppl.* 395 :

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18021, 1994) teaches that the etiology and pathogenesis of chronic inflammatory bowel disease are unknown (see the Abstract). Fox et al (*Infection and Immunity*, April 1999, p. 1757-1762) suggest that *Helicobacter* species are associated with colitis (the Abstract). It is unpredictable as to which microorganisms may be involved in ulcerative colitis. This is evidenced by Macpherson et al (*Gut*, 1996,38:365-375). Macpherson et al suggest that there may be multiple organisms involved in inflammatory bowel disease. Macpherson et al disclose experiments that show that in relapse of inflammatory bowel disease there is a breakdown of tolerance to the normal commensal flora of the gut (which includes multiple organisms). Multiple microorganisms that reside in the gastrointestinal tract are evidenced by Coleman et al, (*Applied and Environmental Microbiology*, October 1996, p. 3632-3639). Coleman et al teach that there are six microbial competitors in the human gastrointestinal tract and they are *Escherichia coli*, *Enterobacter aerogenes*, *Bacteroides ovatus*, *Fusobacterium varium* and *Enterococcus faecalis*. Cross-reactivity is a factor to be considered since there are multiple microorganisms that reside in the gastrointestinal tract. Marx et al (*Infection and Immunity*, June 1982, 36 (3) p. 943-948) teach that cross-reactivity exist between species of the genera *Bacteroides* and species of the genera *Fusobacterium* (see the Abstract). Ushijima et al (*Journal of Medical Microbiology*, September 1990, 33 (10:17-22) further teach that cross-reactivity exists between species of colonic bacteria (see the Abstract). Immunopathogenesis is also associated with ulcerative colitis. Braegger (*Acta Paediatr Suppl.* 395 : 18021, 1994) teaches that immunological mechanisms may play a significant role in mediating the intestinal lesion and some of the systemic

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manifestations of Crohn's disease and ulcerative colitis. Braegger teaches that Crohn's disease and ulcerative colitis present dense infiltration of inflammatory cells, increased plasma cells, T lymphocytes, macrophages and neutrophils (page 18, 1st column). Braegger further teaches that ulcerative colitis may be caused by an IgG-mediated autoimmune process to the colon mucosa (pages 20-21).

Since the detection of antibodies is used in the claimed invention to diagnose ulcerative colitis, one skilled in the art would have to possess the knowledge or be provided with sufficient guidance with regard as to how to detect only the target microorganism (i.e. *Fusobacterium varium*) and not a mixture of colonic bacteria antibodies in order to make a diagnosis of ulcerative colitis. The cited references have shown that unpredictability and uncertainty exists regarding which microorganism or microorganisms are the causative agents of ulcerative colitis. Other references have been cited that show that there are multiple microorganisms that reside in the gastrointestinal tract and references have also been cited to show the immunopathogenesis associated with the disease. Therefore, it can be concluded that undue experimentation would be required to use the claimed method of diagnosing ulcerative colitis without proper guidance.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention.

The specification fails to teach how a sample is obtained? How to determine the amount of antibody significant to make a diagnosis of ulcerative colitis? How to assure that the target antibody (i.e. *Fusobacterium varium*) is obtained and not a mixture of

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antibodies from other colonic bacteria? Nor does the specification provide a correlation between how to diagnosis of ulcerative colitis and the detection of *Fusobacterium varium* antibodies. Therefore, it is unclear as to how to make a diagnosis of ulcerative colitis using the claimed method.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification as to the etiologic agent that causes ulcerative colitis 3) there are limited working examples which suggest the detection of *Fusobacterium varium* antibodies 4) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level), and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

In view of all of the above, in view of the lack of predictability regarding the cross reactivity of microorganisms that inhabit the gastrointestinal tract and uncertainty of the

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etiologic agent of ulcerative colitis in the art, it is determined that it would require undue experimentation to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: 1) providing a sample (i.e sample source, 2) determining that the target antibody (i.e *Fusobacterium varium*) is obtained and not antibodies to a mixture of colonic bacteria, 3) determining the amount of antibody significant to make a diagnosis and 4) the correlation as to how to a diagnose of ulcerative colitis is made using the antibody.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Please note: The Examiner is viewing the method of diagnosing ulcerative colitis as a method of detecting *Fusobacterium varium*.

5. Claim 14 is rejected under 35 U.S.C. 102(b) as anticipated by Danielsson et al (*Scandinavian Journal of Infectious Diseases*, 1979 (19), p. 52-60).

Claim 14 is drawn to a method of diagnosis of ulcerative colitis.

Danielsson et al teach the detection of antibodies of aerobic and anaerobic bacteria including *Fusobacterium varium*. Danielsson et al teach that the strains of bacteria were used as antigens for tube agglutination, passive hemagglutination, indirect immunofluorescence and immune hemolysis assays with serum specimens obtained before and after operation of the patient (see the Abstract).

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material

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method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Pertinent Prior Art

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure (*Onderdonk et al, Infection and Immunity, January 1976, 13(10) and Dragstedt, Diseases of the Colon and Rectum (UNITED STATES) August 1988, 31(8), p. 658-664*).

Status of Claims

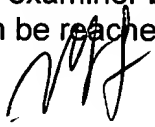
7. No claims are allowed.

Conclusion

8. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.


Vanessa L. Ford
Biotechnology Patent Examiner
April 16, 2002


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